



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

MAR 23 2000

Food and Drug Administration  
Center for Devices and  
Radiological Health  
2098 Gaither Road  
Rockville, MD 20850

WARNING LETTER

VIA FACSIMILE  
VIA FEDERAL EXPRESS

William W. George  
Chairman and Chief Executive Officer  
Medtronic, Inc.  
7000 Central Avenue, N.E.  
Minneapolis, Minnesota 55432

Dear Mr. George:

The Food and Drug Administration's (FDA's) Center for Devices and Radiological Health (CDRH) has reviewed Medtronic, Inc.'s (Medtronic's) Internet website at [www.medtronic.com](http://www.medtronic.com). The site includes a number of significant inappropriate representations pertaining to the company's Activa® Tremor Control System (Activa or Activa System). The Activa Tremor Control System is a device within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). As discussed below, these representations have caused your device to be misbranded within the meaning of section 502(o) and adulterated within the meaning of sections 501(f)(1)(B) and 501(i) of the Act.

CDRH approved Medtronic's premarket approval application, P960009, for the following indication: "unilateral thalamic stimulation for the suppression of tremor in the upper extremity in patients who are diagnosed with essential tremor or Parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability."

Your website makes a claim that "people with bilateral tremor can have two systems implanted, one for each affected side." This is in direct contradiction to the language describing your product's approved intended use, which is noted above. We are aware that FDA's Minneapolis District Office issued Medtronic a warning letter in November 1998. That letter advised you that the agency objected to your changing the Indications section in your product labeling. Your response to the letter said, "Please be aware, Medtronic's failure to quote the indications exactly as they were in the labeling was inadvertent. We certainly agree to use direct quotations on the indications. Originally, Medtronic did not understand that the phrase *"The safety or effectiveness of this therapy has not been established for . . . bilateral stimulation"* needed to be included in every mention of the indication in such labeling. All future labeling for this product will include this phrase in the indication."

Promoting your product for use in bilateral stimulation is inconsistent with a statement that the use of the therapy has not been shown to be safe or effective for bilateral stimulation. We have been advised by the medical review staff in CDRH's

Office of Device Evaluation (ODE) that the agency has not granted marketing approval for the intended use of bilateral stimulation, whether it is with one or two implanted devices and that, in fact, the advisory panel that reviewed Medtronic's original PMA voted that there were insufficient safety data to support the company's bilateral use indication. As you probably are aware, the panel's recommendation was the basis on which CDRH explicitly approved the device for unilateral use only.

The Indications section on your website is as follows: "Unilateral suppression of uncontrolled essential tremor or Parkinsonian tremor in an upper extremity." This does not include the qualification that the indication is based on the tremor's not being adequately controlled by medication and where the tremor constitutes a significant functional disability. Nor does it include the word, "thalamic," and the absence of that limiting term could mislead readers into believing that the device is safe and effective for use in other parts of the brain. These changes constitute changes in the intended use for the device. FDA's regulations at 21 CFR 801.4 provide that the intended use of a device refers to the objective intent of those persons responsible for the device labeling. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the device. This objective intent may, for example, be shown by labeling claims, advertising matter or oral or written statements by such person or their representatives.

Your website contains the following statement of warnings, precautions, and adverse events: "May affect or be affected by medical equipment, e.g., magnetic resonance imaging (MRI), or cardiac pacemakers. Adverse events related to the therapy, device or procedure can include: paresthesia, headache, paresis, dysarthria, disequilibrium, jolting or shocking stimulation, loss of effect, intracranial hemorrhage." The section does not include a statement of the unknown potential for neurotoxicity or carcinogenicity of the lead materials or the possibility of depression and/or suicidal ideation from deep brain stimulation, language that is included in the statement of risks in your product labeling.

The warnings page also does not include a "Use in Specific Populations" section, which provides a number of contraindications for the use of the device. In addition, at least one of your patient testimonials is inconsistent with the "Use of Specific Populations" approved in the product's labeling. The labeling includes a statement that, "The safety and effectiveness of this therapy has not been established for the following" and includes the population "patients with previous thalamotomy or surgical ablation procedure." The testimonial by Gerald Buttleman that appears on Medtronic's website includes a statement that Mr. Buttleman had been previously treated by thalamotomy. While such use may be permitted in the United Kingdom, the promotion of it on your website was not limited to a separate European or UK page, but was included in the company's international survey of beneficial results.

We have also been advised by ODE that Medtronic has not submitted data to support its claim, "Suppress tremor. Restore function." However, the company's website says quite plainly "Suppress tremor. Restore function." Many of the company's testimonials and its other pages state or imply that the device is helpful in restoring daily function and activity and that the device provides results superior to those provided by pharmaceutical options or by other surgical options. In fact, the device is indicated for people in whom pharmaceuticals have not been successful and in patients who have not

had surgery; it is misleading to imply that the device has been demonstrated to provide better results than would the use of drugs or surgery in the same patient.

The publication of the company's February 17, 2000 press release and its posting on your Internet site are also inappropriate. In the press release, the company selectively quoted parts of the study discussed in the New England Journal of Medicine and presented one study's results as being conclusive and established. In fact, the company has not submitted the study results to support the claims that it is drawing as conclusions from the study and presenting as its own. Quoting selected portions of a study is not included within the scope of the recent litigation involving FDA's regulation of the distribution of peer-reviewed journal reprints.

You have included on the website also several references to Benabid *et al.* One of these is a statement that "thalamic stimulation may reduce or eliminate the need for medication. One study showed that one-third of Parkinson's Disease patients reduced their L-Dopa dosage by 30%." Medtronic has not submitted to FDA data to demonstrate that the device is useful in reducing drug use in patients for whom drug therapy is successful and is ongoing.

The conditions of approval for your PMA included the provision that "No advertising or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device." Changing the intended use of your device by promoting it for bilateral use and for use in populations in whom it has not been demonstrated to be safe and effective has resulted in the product's being misbranded within the meaning of section 502(o) of the Act because Medtronic has not submitted to FDA the necessary notice or other information respecting the device, as required by section 510(k) of the Act. Among the required information respecting a device is information to support a labeling change that affects safety and effectiveness. FDA's regulations at section 21 CFR 814.39 provide that after FDA's approval of a PMA, an applicant shall submit a PMA supplement for review and approval by FDA before making a change affecting the safety and effectiveness of the device for which the device has an approved PMA, unless the change is of a type for which FDA has permitted an alternate submission or does not require a submission. Changes for which an application shall submit a PMA supplement include new indications for use of the device and labeling changes if they affect the safety or effectiveness of the device. The intended use and other labeling claims that you have made have changed the safety and effectiveness of the device and are not, therefore, permitted until FDA has approved a PMA supplement.

Your claims have resulted in the product's being adulterated within the meaning of section 501(f)(1) because it is a class III device without an approved PMA. They have resulted further in the device's being adulterated within the meaning of section 501(i) because Medtronic is currently conducting under approved investigational device exemptions (IDE's) clinical trials for bilateral use of the device and use of the device in other parts of the brain. The IDE regulations at 21 CFR 812.7 prohibit any sponsor or investigator or any person working on behalf of such sponsor or investigator from representing that the device is safe or effective for the use for which it is being investigated.

This letter is not intended to be an all-inclusive list of deficiencies associated with Medtronic's devices. It is your responsibility to ensure adherence to each requirement of the Act and the regulations. The specific violations noted in this letter may also be reflected in other promotion and advertising materials used by your company. You are responsible for investigating and reviewing all materials to ensure compliance with applicable regulations.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in FDA's initiating regulatory action without further notice. These actions include, but are not limited to, seizure, injunction and/or civil money penalties.

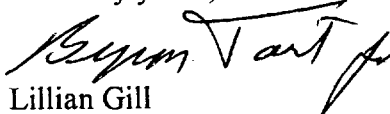
Please notify this office in writing, within 15 working days of your receipt of this letter, of the specific steps that you have taken to correct the noted violations. Your response should include steps being taken to address any misleading information currently in the marketplace and to prevent similar violations in the future. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the timeframe within which the corrections will be completed.

Direct your response to Deborah Wolf, Regulatory Counsel, Promotion and Advertising Policy Staff (HFZ-302), Office of Compliance, Center for Devices and Radiological Health, 2098 Gaither Road, Rockville, Maryland 20850.

A copy of this letter is being sent to FDA's Minneapolis District Office. Please send a copy of your response to the District Director, Minneapolis District Office, Food and Drug Administration (HFR-MW340), 240 Hennepin Ave., Minneapolis, MN 55401-1912.

In addition to the charges made above, the Center is aware that you may be distributing other inappropriate materials. In its review of the materials accompanying your 1999 annual report, ODE found, in many of the pieces reviewed, significant departures from the approved labeling and product information. We are not able to ascertain whether you are currently distributing these materials. Please direct to the abovementioned CDRH headquarters address, pursuant to 21 CFR 807.31(a)(2), representative samples of current advertising and promotional labeling.

Sincerely yours,



Lillian Gill  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health